

WHAT IS CLAIMED IS:

1. A method of examining a reactivity of a first sample with a plurality of second samples having different properties from one another, comprising the 5 steps of:

preparing a substrate with said first sample bound thereto in a defined region;

arranging said plurality of second samples within said region independently of one another; and

10 testing the reactivity of said first sample with each of said second samples.

2. The examination method according to claim 1, wherein said reactivity is a bonding capability between 15 said first sample and said second samples.

3. The examination method according to claim 2, wherein said bonding capability is based on complementation of nucleic acid strands.

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4. The examination method according to claim 1, wherein said first sample is originated from an organism, and said second samples have known properties.

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5. The examination method according to claim 4, wherein said second samples are synthesized.

6. The examination method according to claim 5,
wherein said first sample includes a nucleic acid
originated from an organism and having an unknown base
sequence, and said second samples include synthesized
5 nucleic acids having known base sequences.

7. The examination method according to claim 6,
wherein said first sample includes a set of mRNAs
extracted from an organism.

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8. The examination method according to claim 6,
wherein said first sample includes a cDNA library
synthesized based on mRNAs extracted from an organism.

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9. The examination method according to claim 4,
wherein said first sample includes a nucleic acid
originated from an organism and having an unknown base
sequence, and said second samples include synthesized
chemicals.

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10. The examination method according to claim 4,
wherein said first sample includes a nucleic acid
originated from an organism and having an unknown base
sequence, and said second samples include purified
25 proteins.

11. The examination method according to claim 1,

wherein said first sample has a known property, and
said second samples are originated from an organism.

12. The examination method according to claim 11,
5 wherein said first sample includes a gene having a
known sequence.

13. The examination method according to claim 11,
wherein said first sample includes a cloned oncogene
10 fragment, and said second samples include nucleic acids
originated from an organism.

14. The examination method according to claim 1,
wherein said first sample includes a protein fragment
15 extracted from an organism, and said second samples
include purified proteins of a single type.

15. The examination method according to claim 1,
wherein said first sample includes a purified protein
20 of a single type, and said second samples include
protein fragments extracted from an organism.

16. The examination method according to claim 4,
wherein said first sample includes a protein fragment
25 originated from an organism, and said second samples
include synthesized chemicals.

17. The examination method according to claim 4, wherein said first sample includes a purified protein of a single type, and said second samples include synthesized chemicals.

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18. The examination method according to claim 1, wherein said first sample includes a synthesized chemical, and said second samples include nucleic acids extracted from an organism.

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19. The examination method according to claim 1, wherein said first sample includes a synthesized chemical, and said second samples include protein fragments extracted from an organism.

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20. The examination method according to claim 1, wherein said first sample is comprised of a plurality of samples having different properties, and each of said plurality of samples is bound to one of 20 partitioned regions forming a matrix on the substrate.

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21. The examination method according to claim 20, wherein said first sample includes nucleic acids originated from different biological species, tissues or cells.

22. The examination method according to claim 20,

wherein said first sample includes proteins extracted from different biological species, tissues or cells.

23. The examination method according to claim 20,
5 wherein the density of said matrix is 400/cm² or lower.

24. The examination method according to claim 20,
wherein an array of spots of said second samples is
arranged in each of said partitioned regions in a
10 common arrangement.

25. The examination method according to claim 1,
wherein said substrate is made of glass.

15 26. The examination method according to claim 1,
wherein said first sample is fixed on the substrate by
electrostatic bonds.

27. The examination method according to claim 1,
20 wherein said first sample is fixed on the substrate by
covalent bonds.

28. The examination method according to claim 27,
wherein said first sample is bound to said substrate
25 through a chemical reaction of maleimide groups
introduced to a glass surface of the substrate with
thiol groups possessed by said first sample.

29. The examination method according to claim 28, wherein said first sample includes a protein, and said thiol groups are cycsteine groups of the protein.

5 30. The examination method according to claim 28, wherein said maleimide groups are introduced by introducing amino groups to the glass surface and then reacting said amino groups with N-(6-maleimidocaproyloxy)succinimide.

10 31. The examination method according to claim 28, wherein said maleimide groups are introduced by introducing amino groups to the glass surface and then reacting said amino groups with succinimidyl 4-maleimidophenyl)butyrate.

15 32. The examination method according to claim 28, wherein said chemical reaction is a reaction between an epoxy group introduced to the glass surface of the substrate and an amino group possessed by said first sample.

20 33. The examination method according to claim 30, wherein said amino group is an amino group existing in a nucleic acid base.

25 34. The examination method according to claim 1,

wherein said substrate has a surface previously partitioned by a wall member to define sections forming a matrix, and biological samples having different properties are previously bound to the respective 5 sections as the first sample.

35. The examination method according to claim 34, wherein each of said sections has a hydrophobic wall portion and a hydrophilic bottom portion.

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36. The examination method according to claim 35, wherein said wall member has a thickness in the range of 1 to 20 μm .

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37. The examination method according to claim 1, wherein said second samples are arranged as spots with a diameter of 200 μm or smaller.

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38. The examination method according to claim 1, wherein said second samples are arranged as spots with a density of $400/\text{cm}^2$ or higher.

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39. The examination method according to claim 1, wherein said second samples are supplied by an ink-jet method.

40. The examination method according to claim 39,

wherein said second samples supplied by the ink-jet method include nucleic acids having a base pair length in the range of 2 to 5000 pairs.

5 41. The examination method according to claim 40, wherein said nucleic acids supplied by the ink-jet method are supplied as an aqueous solution having a concentration in the range of 0.05 to 500 μ M.

10 42. The examination method according to claim 39, wherein said ink-jet method is a bubble jet method.

15 43. The examination method according to claim 1, wherein each of said second samples is supplied by contacting a pin with a solution of the sample and contacting said pin physically with said substrate.

20 44. The examination method according to claim 1, wherein each of said second samples is supplied by sucking a solution of the sample using a capillary and then contacting the tip of said capillary physically with the substrate.

25 45. A biological sample matrix, wherein two or more biological samples of different origins are bound to respective partitioned regions forming a matrix on a substrate.

46. The biological sample matrix according to
claim 45, wherein said biological samples include
cloned oncogene fragments.

5 47. The biological sample matrix according to
claim 45, wherein said biological samples include
mRNAs.

10 48. The biological sample matrix according to
claim 45, wherein said biological samples include
cDNAs.

15 49. The biological sample matrix according to
claim 45, wherein said biological samples include a
CDNA library.

20 50. The biological sample matrix according to
claim 45, wherein said biological samples include two
or more types of proteins having different
conformations.

51. The biological sample matrix according to
claim 45, wherein the density of said matrix is 400/cm²
or lower.

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52. The biological sample matrix according to
claim 45, wherein said substrate is made of glass.

53. The biological sample matrix according to
claim 45, wherein said biological samples are fixed on
the substrate by electrostatic bonds.

5 54. The biological sample matrix according to
claim 45, wherein said biological samples are fixed on
the substrate by covalent bonds.

10 55. The biological sample matrix according to
claim 54, wherein said biological samples are bound to
said substrate through a chemical reaction of maleimide
groups introduced to a glass surface of the substrate
with thiol groups possessed by said biological samples.

15 56. The biological sample matrix according to
claim 55, wherein said biological samples include
proteins bound to the glass surface through a chemical
reaction of maleimide groups introduced to the glass
surface with thiol groups of cysteine residue of the
20 protein.

25 57. The biological sample matrix according to
claim 55, wherein said maleimide group is introduced by
introducing amino groups to the glass surface and then
reacting said amino groups with N-(6-
maleimidocaproyloxy)succinimide.

58. The biological sample matrix according to
claim 55, wherein said maleimide group is introduced by
introducing amino groups to the glass surface and then
reacting said amino groups with succinimidyl 4-
5 (maleimidophenyl)butyrate.

59. The biological sample matrix according to
claim 54, wherein said biological samples include
nucleic acids bound to said substrate through a
10 chemical reaction of epoxy groups introduced to a glass
surface of the substrate with amino groups possessed by
said nucleic acids.

60. The biological sample matrix according to
15 claim 45, wherein said two or more biological samples
are supplied on the respective partitioned regions on
the substrate by an ink-jet method.

61. The biological sample matrix according to
20 claim 45, wherein said substrate has a surface
partitioned by a wall member to define sections forming
a matrix, and said two or more biological samples of
different origins are bound to the respective sections.

25 62. The biological sample matrix according to
claim 61, wherein each of said sections has a
hydrophobic wall portion and a hydrophilic bottom

portion.

63. The biological sample matrix according to
claim 62, wherein said wall member has a thickness in
5 the range of 1 to 20 μm .

64. A method of detecting a complex formed
between an oligonucleotide of which base sequence is
known and a component having a capability of binding to
10 said oligonucleotide, comprising the steps of:

preparing at least one oligonucleotide of which
base sequence is known;

preparing at least two liquid test samples
potentially containing a component having a capability
15 of binding to said oligonucleotide;

binding said oligonucleotide as a probe to a
predetermined region on a solid substrate to produce a
detection substrate;

20 arranging a plurality of spots of said test
samples at a predetermined amount to form an array of
said test samples within said region with said
oligonucleotide bound thereto;

25 detecting whether a complex between said
oligonucleotide and said component is present or not
for each of said plurality of spots; and

determining whether or not said component is
contained in each of said liquid test samples, or how

strong its binding capability to said oligonucleotide is, based on said detection.

65. The detection method according to claim 64,
5 wherein said oligonucleotide bound to said detection substrate has a base sequence with a base length of 2 to 100.

66. The detection method according to claim 64,
10 wherein said liquid test samples are solutions each containing at least one nucleic acid of which base sequence is unknown, detection is made whether a complex between said oligonucleotide and said nucleic acid is formed or not for each of said test samples to thereby determine whether or not said nucleic acid contains a base sequence complementary to the known base sequence of said oligonucleotide functioning as said component having a capability of binding to said oligonucleotide.

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67. The detection method according to claim 66, wherein said nucleic acid contained in each of said liquid test samples includes a set of mRNAs extracted from an organic tissue.

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68. The detection method according to claim 66, wherein said nucleic acid contained in each of said

liquid test samples includes a cDNA library prepared based on a set of mRNAs extracted from an organic tissue.

5 69. The detection method according to claim 66, wherein said nucleic acid contained in each of said liquid test samples has a base length of 2 to 5000.

10 70. The detection method according to claim 64, wherein said liquid test samples are solutions each containing at least one protein, the proteins contained in said test samples being different from one another.

15 71. The detection method according to claim 64, wherein said liquid test samples are solutions each containing at least one chemical, the chemicals contained in said test samples being different from one another.

20 72. The detection method according to claim 64, wherein said liquid test samples are extracts from different biological species, tissues or cells.

25 73. The detection method according to claim 64, wherein a plurality of oligonucleotides having known base sequences different from one another are used as a probe, and said detection substrate has a plurality of

predetermined sections arranged in a matrix form to which said oligonucleotides are to be bound, respectively.

5 74. The detection method according to claim 73, wherein said plurality of oligonucleotides are bound to said sections to constitute a matrix at a density of 400/cm² or lower, said sections having the same area as one another.

10 75. The detection method according to claim 73, wherein said test samples are spotted in an array form in each of said sections to which said plurality of oligonucleotides having known base sequences different from one another are bound so that the spot positions in each section are arranged in the same way as one another.

20 76. The detection method according to claim 64, wherein said solid substrate used as said detection substrate is made of glass.

25 77. The detection method according to claim 64, wherein said oligonucleotide is fixed on the detection substrate by covalent bonds.

78. The detection method according to claim 77,

wherein said oligonucleotide is fixed on the detection substrate by covalent bonds formed through a chemical reaction of maleimide groups introduced to a glass surface of the substrate used as said solid substrate
5 with thiol (-SH) groups possessed by said oligonucleotide.

79. The detection method according to claim 78, wherein said maleimide groups introduced to the glass
10 surface is formed by first introducing amino groups to the glass surface and then reacting N-(6-maleimidocaproyloxy)succinimide with the amino groups.

80. The detection method according to claim 78, wherein said maleimide groups introduced to the glass
15 surface is formed by first introducing amino groups to the glass surface and then reacting succinimidyl 4-(maleimidophenyl)butyrate with the amino groups.

20 81. The detection method according to claim 77, wherein said oligonucleotide is fixed on the detection substrate by covalent bonds through a chemical reaction of epoxy groups introduced to a glass surface of the substrate used as said solid substrate with amino
25 groups possessed by said oligonucleotide.

82. The detection method according to claim 64,

wherein said detection substrate has a surface previously partitioned to form a plurality of sections, and two or more different types of oligonucleotides of which base sequences are known are previously bound to 5 the sections, respectively, in a matrix form.

83. The detection method according to claim 82, wherein said sections previously formed on the surface of said detection substrate are separated from each 10 other by a wall member and each section having a hydrophobic wall portion and a hydrophilic bottom portion section is hydrophilic.

84. The detection method according to claim 83, 15 wherein said wall member has a thickness in the range of 1 to 20 μm .

85. The detection method according to claim 64, wherein each of the spots of said two or more test 20 samples formed in each section has a diameter of 200 μm or lower.

86. The detection method according to claim 64, wherein the spots of said two or more test samples 25 formed in each section is arranged at a density of 400/ cm^2 or smaller.

87. The detection method according to claim 64,
wherein each of the spots of said two or more test
samples is formed by supplying a predetermined amount
of a solution of said test samples by an ink-jet
5 method.

88. The detection method according to claim 87,
wherein said two or more test samples are spotted by an
ink-jet method as a solution containing a nucleic acid
10 with base length of 100 to 5000, respectively.

89. The detection method according to claim 88,
wherein said two or more test samples are spotted by an
ink-jet method as a solution containing a nucleic acid
15 as a total concentrations of 0.05 to 500 μ M,
respectively.

90. The detection method according to claim 88,
wherein said ink-jet method used for spotting is a
20 bubble jet method.

91. The detection method according to claim 64,
wherein the spots of test samples are formed by
contacting a pin having a tip for collecting sample
25 solutions with a solution of each test sample to allow
the sample solution to adhere to the tip of said pin
for taking a predetermined amount of the solution and

then physically contacting the tip of said pin with a surface of the substrate to transfer said predetermined amount of the solution to the substrate surface.

5 92. The detection method according to claim 64, wherein the spots of test samples are formed by sucking a solution of each test sample using a capillary having a tip for sucking sample solutions thereinto and then physically contacting the tip of said capillary with a 10 surface of the substrate to transfer a predetermined amount of the solution to the substrate surface.

15 93. A detection substrate with two or more oligonucleotides having known base sequences different from one another fixed on a solid substrate,

20 wherein said two or more oligonucleotides are bound and fixed on a plurality of predetermined sections, respectively, so that one oligonucleotide is present in each section, and said plurality of predetermined sections with oligonucleotides fixed therein are arranged in a matrix form on a surface of said solid substrate.

25 94. The detection substrate according to claim 93, wherein the known base sequence of each of said two or more oligonucleotides bound in predetermined sections has a base length of 2 to 60.

95. The detection substrate according to claim 93, wherein said plurality of predetermined sections are arranged in a matrix form on the surface of said solid substrate at a density of 400/cm² or lower.

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96. The detection substrate according to claim 93, wherein said solid substrate is a glass substrate.

10 97. The detection substrate according to claim 93, wherein said oligonucleotides are fixed on the substrate surface by covalent bonds.

15 98. The detection substrate according to claim 97, wherein said oligonucleotides are fixed on the detection substrate by covalent bonds formed through a chemical reaction of maleimide groups introduced to a glass surface of the solid substrate with thiol groups possessed by said oligonucleotides.

20 99. The detection substrate according to claim 98, wherein said maleimide groups introduced to the glass surface are formed by first introducing amino groups to the glass surface and then reacting succinimidyl 4-(maleimidophenyl)butyrate with the amino 25 groups.

100. The detection substrate according to claim

98, wherein said maleimide groups introduced to the glass surface are formed by first introducing amino groups to the glass surface and then reacting N-(6-maleimidocaproyloxy)succinimide with the amino groups.

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101. The detection substrate according to claim 97, wherein said oligonucleotides are fixed on the detection substrate by covalent bonds through a chemical reaction of epoxy groups introduced to a glass 10 surface of the solid substrate with amino groups possessed by said oligonucleotides.

102. The detection substrate according to claim 93, wherein said two or more oligonucleotides are fixed 15 in each of said predetermined sections such that one oligonucleotide is present in each section by supplying said two or more oligonucleotides in each of said predetermined sections in a matrix form by printing them by an ink-jet process.

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103. The detection substrate according to claim 93, wherein said two or more oligonucleotides are bound to said plurality of predetermined sections previously partitioned in a matrix form.

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104. The detection substrate according to claim 103, wherein said sections previously formed in a

matrix form on the substrate surface are separated from each other by a wall member and each section has a hydrophobic wall portion and a hydrophilic bottom portion.

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105. The detection substrate according to claim 104, wherein said wall member has a thickness in the range of 1 to 20 μm .

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106. The detection substrate according to claim 104, wherein two or more oligonucleotides are fixed to said previously formed sections in a matrix form by an ink-jet method so that said two or more oligonucleotides are supplied only on the bottom portion of each section.

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107. A method of preparing a detection substrate with two or more oligonucleotides having known base sequences different from one another fixed on a solid substrate, comprising:

preparing a solid substrate having a surface previously partitioned into a plurality of sections in a matrix form,

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supplying a predetermined amount of two or more oligonucleotides in said predetermined sections so that only one type of said oligonucleotides is present in each section by an ink-jet method, and

fixing the supplied oligonucleotides in the
predetermined sections.